Complete Summary

GUIDELINE TITLE

Nausea and vomiting.

BIBLIOGRAPHIC SOURCE(S)

Editorial Board Palliative Care: Practice Guidelines. Nausea and vomiting. Utrecht, The Netherlands: Association of Comprehensive Cancer Centres (ACCC); 2006 Jan 12. 28 p. [73 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- September 17, 2007, Haloperidol (Haldol): Johnson and Johnson and the U.S. Food and Drug Administration (FDA) informed healthcare professionals that the WARNINGS section of the prescribing information for haloperidol has been revised to include a new Cardiovascular subsection.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Nausea and vomiting in palliative care patients

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nursing
Oncology
Pharmacology
Psychology

INTENDED USERS

Allied Health Personnel
Nurses
Pharmacists
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians

GUIDELINE OBJECTIVE(S)

To improve the quality of palliative care for the individual patient by providing recommendations regarding diagnosis and treatment. Secondarily, these guidelines can be used:

- As an aid during consultations regarding palliative care
- To increase knowledge regarding palliative care
- For training and continuing education

TARGET POPULATION

Cancer patients who experience nausea and vomiting

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Patient history

2. Physical examination (including dehydration and bowel obstruction assessment)
3. Blood tests (renal and hepatic function, electrolytes, drug concentrations)
4. Diagnostic imaging (x-ray, ultrasound, computed tomography (CT), magnetic resonance imaging, gastroscopy

Management/Treatment

1. Integral approach to management
    - Provision of information to patient
    - Communication
    - Supportive care
    - Continuity of care
2. Treatment of the underlying cause
3. Nonpharmacological symptom management
    - General and nutritional advice
    - Administration of fluids and electrolytes
    - Gastric tube
    - Psychosocial techniques
4. Pharmacological treatment of symptoms with antiemetics
    - Dopamine antagonists (metoclopramide, haloperidol, levomepromazine)
    - Prokinetic drugs (metoclopramide, domperidone, erythromycin
    - Serotonin (5HT3) antagonists (ondansetron granisetron, tropisetron)
    - Neurokinin antagonists (aprepitant)
    - Corticosteroids (dexamethasone)
    - Antihistamines (cyclizine, levomepromazine)
    - Anticholinergic agents (cyclizine, butylscopolamine, levomepromazine)
    - Octreotide/lanreotide

MAJOR OUTCOMES CONSIDERED

- Rate of symptom relief
- Quality of life
- Side effects of pharmacological agents

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level 1 = Based on a systematic review or at least two randomised trials of sufficient quality

Level 2 = Based on at least two comparative clinical trials of moderate quality or insufficient size, or other comparative studies

Level 3 = Based on one comparative trial or a non-comparative trial

Level 4 = Based on expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The level of evidence was determined using a classification system that conforms to that of the CBO (Centraal Begeleidings Orgaan). The levels of evidence reflect the opinions of the authors and are open to discussion.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

No pretence was made to create evidence-based guidelines in the same sense that the CBO guidelines are evidence-based. The methods required to develop evidence-based guidelines made the approach unfeasible given the time and financial restrictions placed on the editorial staff

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Diagnosis

Patient History

- Medical history
- Presence, duration, course, and severity of nausea
- Frequency and amount of retching and/or vomiting; characteristics and odour; presence of food remnants and/or blood in vomit; relation to mealtimes
- Relationship (or lack thereof) between nausea and vomiting; improvement of nausea after vomiting
- Induction of nausea/vomiting by factors such as meals, change in position or movement, recent radiotherapy or chemotherapy
- Use of antiemetics and their effects
- Associated symptoms, such as anorexia, difficulty swallowing or digesting, stomach pain, early satiety, abdominal pain or cramps, swollen abdomen, stomach rumbling, constipation, thirst, polyuria, pain, cough, hiccups, dizziness, hearing impairment, headache, or neurological impairment
- Changes in body weight
- Anxiety, stress, or depression and their effect on symptoms
- Alcohol use
- (Changes in) medication

The history can provide important information regarding the cause of nausea and/or vomiting:

- Regurgitation of undigested, non-acidic food directly after swallowing indicates an oesophageal disorder
- Vomit large amounts several hours after eating, often accompanied by hiccups, indicates delayed gastric emptying caused by partial obstruction of the pylorus or duodenum
- Severe vomiting, which can lead to rapid dehydration, indicates a total pyloric or duodenal obstruction, which is uncommon
- Small amounts of vomit with no signs of gastric retention are consistent with a filled gastric cavity caused by tumour or external compression
- Small amounts of vomit with varying degrees of nausea and fluid associated with abdominal swelling indicates gastroparesis
- Vomiting combined with increased abdominal girth and shortness of breath can indicate ascites

- Position-dependent nausea and vomiting may be caused by fluid stasis in the stomach, infiltration of the mesenterium/peritoneum, or hypersensitivity of the vestibular apparatus (caused by tumours of the inner or middle ear or as a rare side effect of opioids)
- Vomiting, often in the morning, in the absence of nausea, combined with headache and/or neurological defects, indicates increased intracranial pressure
- Vomiting combined with thirst, polyuria, constipation, drowsiness, and/or confusion may indicate hypercalcaemia

Physical Examination

- General: nutritional status, hydration status, mental condition
- Inspection of the mouth and pharynx, particularly for candidiasis
- Abdominal examination: surgical scars, peristalsis, signs of ascites (shifting dullness = position-dependent dullness during percussion, undulation = fluid wave induction in the flanks), distended stomach (clapotage = sloshing sound when the gastric region is pressed), liver enlargement, abnormal resistance, pain when pressure is applied, rectal examination
- Fundoscopy/neurological examination if increased intracranial pressure is suspected
- Vomit inspection. Large amounts of food remnants indicate pyloric or duodenal obstruction or bowel obstruction

Additional Tests

If desired, additional tests can be performed as indicated:

- Blood analysis:
    - Serum creatinine or serum potassium to determine the degree of dehydration, renal impairment, and/or potassium loss
    - Total calcium (correct for low serum albumin using the formula Corrected Ca = serum calcium + 1.0 (0.025 x serum albumin) or Ca^{2}+ (correction is not necessary for low serum albumin) to assess for hypercalcaemia
    - Hepatic function (bilirubin, alkaline phosphatase [AP], gamma-glutamyl transpeptidase [gamma-GT], aspartate aminotransferase [ASAT], alanine aminotransferase [ALAT]): if liver metastases are suspected
    - Sodium levels: if hyponatraemia is suspected
    - Concentrations of digoxin, anti-epileptics, and theophylline if used
- Diagnostic imaging:
    - Abdominal X-ray if constipation or bowel obstruction is suspected
    - Abdominal ultrasound or computed tomography (CT) scan if gastric obstruction, liver metastases, ascites, or carcinomatous peritonitis is suspected
    - CT scan or magnetic resonance imaging (MRI) of the brain if metastases or meningitis carcinomatosa is suspected
- Perform gastroscopy if gastritis, ulcer, or gastric compression or obstruction is suspected

Management

Integral Approach

Information

- Provide information regarding the cause of nausea and vomiting, relevant factors, and the expected duration. The potential risks, symptoms, and consequences of dehydration should also be mentioned
- Provide information regarding the goals, effects, and possible side effects of treatment with antiemetics
- Advise on the (limited) role of administering parenteral fluids

Communication

- Ascertain whether the patient is experiencing anxiety, stress, or other psychogenic factors
- Discuss the changing role of nutrition (given its importance in relation to the prognosis) with the patient and his or her caregivers
- Discuss the use of a symptom diary to aid in communication

Supportive Care

- Ascertain whether nutritional advice from a dietician is needed
- Discuss the value of relaxation and distraction techniques if anxiety is suspected to play a role. For treatment, contact can be made with a physiotherapist (relaxation and massage), psychologist (relaxation and hypnosis), or music therapist (relaxation and distraction)
- Consider pharmacological support with anxiolytics for anxiety and stress

Continuity of Care

- Ensure effective communication between various care providers
- For complementary care, consider forms that the patient can receive or practice primarily at home (or in hospital), possibly with support from a volunteer aid

Treating the Cause

Treating the Underlying Cause

- Targeted antitumour therapy (surgery, radiotherapy, or chemotherapy) should be considered only if there is a reasonable chance of response and a low risk of severe side effects
- Dose modification or, if necessary, discontinuation; for opioids, consider opioid rotation or trying an alternative route of administration
- For patients with obstruction of the gastric outlet or duodenum:
    - If life expectancy is measured in weeks or months, stent placement may be considered
    - If life expectancy is a few months or more, gastrojejunostomy can be considered
- Treatment of peptic ulcer, gastritis, pancreatitis, cholelithiasis, nephrolithiasis, constipation, pain, or cough

- Treatment of electrolyte disorders:
    - Hypercalcaemia: zoledronic acid 4 mg intravenous (i.v.) or aminohydroxypropylidine bisphosphonate (APD) 90 mg i.v. + 3 to 4 litres of 0.9% NaCl/24 hours (see guideline on hypercalcaemia); this often implies hospital admission for fluid administration
    - Hyponatraemia: water restriction (for syndrome of inappropriate antidiuretic hormone secretion [SIADH]) or broth orally/0.9% NaCl i.v. (if there is concurrent dehydration)
- For ascites, consider ascites puncture and drainage
- For bowel obstruction (see also the Association of Comprehensive Cancer Centres (ACCC) guideline on bowel obstruction):
    - Discuss the feasibility and desirability of surgery with the surgeon
    - If surgery is not an option, consider conservative therapy:
        - Gastric drainage (nasogastric tube) as needed during the acute phase, particularly for severe vomiting
        - Somatostatin analogues: octreotide 100 to 300 microgram subcutaneous (s.c.) three times daily or 300 to 900 microgram/24 hours continuous s.c. or i.v. infusion (particularly for severe vomiting); or, during the stable phase after the efficacy of octreotide has been confirmed, lanreotide PR 30 mg i.m. once every 2 weeks
        - Butylscopolamine 60 to 120 mg/24 hours s.c. or i.v.
        - For persistent nausea and vomiting despite pharmacological therapy, continuous gastric drainage with the use of nasogastric tube or percutaneous endoscopic gastrostomy (PEG) tube
- For brain metastases, corticosteroids (dexamethasone 4 mg/day p.o., s.c., or i.v.; if necessary higher doses can be given, see guideline on Brain Metastases) and possibly radiotherapy

Non-pharmacological

Non-pharmacological Treatment of Symptoms

<u>General and Nutritional Advice</u>

- Keep tissues and water to rinse the mouth nearby
- Maintain a calm environment and fresh air
- Wear loose clothing
- Avoid strong perfumes
- Avoid the sight and smell of food; immediately remove any food that the patient cannot or will not eat
- Practice proper mouth care
- Sit in an upright position for 30 to 45 minutes after eating
- Take small, frequent meals; avoid foods that are greasy, warm, spicy, or aromatic; in some cases food is best served cold; allow the patient to eat what he or she finds appetising and tolerates well
- Drink cola (not too cold!)
- Suck on an ice cube, sorbet, or a piece of frozen fruit (pineapple, kiwi, or apple)
- For patients with severe vomiting, try to ensure that the stomach is full, provided that gastric retention has been ruled out

- Consider consulting a dietician
- For malnourished patients, consider dietary supplements; however, these are often poorly tolerated and may sometimes exacerbate symptoms

Administration of Fluids and Electrolytes

If there are indications of dehydration based on the patient history, physical examination, and possibly laboratory assessment, parenteral fluid administration can be considered, depending on the life expectancy and the wishes of the patient; for cases of hypokalaemia, supplemental potassium can be given intravenously.

Gastric Tube

Gastric tubes have a limited role in the palliative phase, except in cases of total pyloric or duodenal obstruction, bowel obstruction, or untreatable gastroparesis. For non-responsive vomiting in these situations, a nasogastric or percutaneous endoscopic gastrostomy (PEG) tube can be used to drain off stomach contents, thereby preventing vomiting.

Psychological Techniques

Psychological techniques are used to manage nausea and vomiting primarily when psychogenic factors (anxiety and stress) and conditioning (anticipatory nausea and vomiting) are found to play an important role. These types of nausea and vomiting respond poorly to antiemetics. Psychological techniques act by inducing relaxation, distraction, and/or a feeling of self-control. Instruction from a psychologist is necessary the first time, after which a physician, nurse, or even the patient can usually apply the technique on their own.

The following techniques can be applied:

- Distraction
- Relaxation techniques
- Guided imagery
- Systematic desensitisation
- Self hypnosis
- Biofeedback
- Music therapy

The approach used must be attuned to the coping style of the patient. Some patients will benefit more from a physical approach aimed at relaxation, while others may respond to a more active approach involving behavioural therapy.

Pharmacological

Pharmacological Treatment of Symptoms

Knowledge of the aetiology is essential for applying targeted antiemetic therapy. Antiemetics can be administered by oral, rectal, transdermal, or parenteral routes.

For chronic nausea (which is often associated with delayed gastric emptying and vomiting) antiemetics must be given rectally or possibly parenterally.

Some agents have multiple mechanisms of action and interact with various neurotransmitters.

Agents used as antiemetics are shown in Table 1 in the original guideline document:

- Dopamine antagonists: inhibit central dopamine (D2) receptors in the chemoreceptor trigger zone (metoclopramide, haloperidol, levomepromazine)
- Prokinetic drugs: promote gastric emptying by inhibiting dopamine receptors in the stomach (metoclopramide, domperidone, erythromycin); metoclopramide also stimulates peripheral 5HT4 receptors, which increases acetylcholine secretion from the myenteric plexus and promotes peristalsis
- Serotonin (5HT3) antagonists (ondansetron, granisetron, tropisetron)
- Neurokinin antagonists (aprepitant)
- Corticosteroids (dexamethasone)
- Antihistamines (cyclizine, levomepromazine)
- Anticholinergic agents (cyclizine, butylscopolamine, levomepromazine)
- Octreotide/lanreotide (analogues of somatostatin, a gastrointestinal hormone that inhibits secretion in the gastrointestinal tract)

The choice of antiemetic depends on the mechanism that lead to nausea and vomiting and on the receptors involved:

- Prokinetic drugs (metoclopramide or domperidone, possibly erythromycin) for gastritis or gastric fluid stasis
- Metoclopramide or haloperidol for nausea and vomiting caused by pharmacological stimulation of the chemoreceptor trigger zone (particularly opioids), hypercalcaemia, or renal insufficiency
- Serotonin (5HT3) antagonists (possibly in combination with dexamethasone) for nausea and vomiting following surgery, radiotherapy, or chemotherapy (only during the first 24 hours)
- Aprepitant for nausea and vomiting following chemotherapy
- Corticosteroids for nausea induced by chemotherapy (in combination with serotonin antagonists) or increased intracranial pressure, or nausea resistant to other antiemetics
- Cyclizine or scopolamine patch for vestibular causes of nausea and vomiting
- Octreotide/lanreotide and/or butylscopolamine for conservative treatment of bowel obstruction
- Levomepromazine, serotonin antagonists, or olanzapine for nausea and vomiting that is refractory to other treatments

Approximately 30% of cases will require a combination of different antiemetics.

Parenteral administration of the following agents may be considered for persistent vomiting when rectal administration is not available or feasible:

- Metoclopramide 40-100 mg/24 hours s.c. or i.v. as continuous infusion
- Haloperidol 2-5 mg/24 hours s.c. or i.v. as continuous infusion
- Dexamethasone 2-4 mg once daily s.c. (preferably not as continuous infusion)

- Ondansetron 16 mg/24 hours s.c. or i.v.
- Levomepromazine 3.25-25 mg s.c. a.n. or as continuous infusion

With the exception of dexamethasone, the aforementioned agents may be easily combined with other agents (e.g., morphine) in one solution. The disadvantages to this approach, however, are that the dose of each agent can no longer be adjusted individually and bolus injection is not possible. Given that metoclopramide and haloperidol are both dopamine antagonists, combining these agents for the treatment of nausea is not rational. If given for the treatment of delirium, haloperidol may be added to metoclopramide. However, this is associated with an increased risk of developing extrapyramidal symptoms.

NB: Cannabis (in cigarettes or tea or as tetrahydrocannabinol [THC]) has a limited role in treating nausea and vomiting, particularly for chemotherapy-induced nausea and vomiting. It is not generally recommended due to its side effects, such as dysphoria, particularly in elderly patients.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not identified or graded for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management and treatment of nausea and vomiting in cancer patients, to improved quality of life and prevent morbidity.

POTENTIAL HARMS

Side effects of antiemetics

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The duration of the palliative phase can vary from weeks to years; therefore, the guideline is in no way limited to the terminal phase. The applicability and relevance of the diagnostic and treatment options discussed in these guidelines are highly dependent on the phase of the disease process and life expectancy. Care providers who make use of this guideline must therefore determine which of the diagnostic and treatment options mentioned in the guideline are applicable to

his or her working environment, specialty, and the individual situation of the patient in question.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Foreign Language Translations
Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Editorial Board Palliative Care: Practice Guidelines. Nausea and vomiting. Utrecht, The Netherlands: Association of Comprehensive Cancer Centres (ACCC); 2006 Jan 12. 28 p. [73 references]

ADAPTATION

The first version of the guideline on nausea and vomiting was written in 1996 as part of the guideline on palliative care developed by the Comprehensive Cancer Centre Middle Netherlands (Integraal Kankercentrum Midden-Nederland, IKMN). The current version was revised in cooperation with the Palliative Care Working Group of the Comprehensive Cancer Centre Middle Netherlands and the Quapal Working Group of the Comprehensive Cancer Centre East (Integraal Kankercentrum Oost, IKO) in 2005.

DATE RELEASED

2006 Jan

GUIDELINE DEVELOPER(S)

Association of Comprehensive Cancer Centres - Disease Specific Society

SOURCE(S) OF FUNDING

Association of Comprehensive Cancer Centres

GUIDELINE COMMITTEE

Editorial Board Palliative Care: Practice Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

The Editorial Board Palliative Care: Practice Guidelines Members: A. de Graeff, medical oncologist, University Medical CentreUtrecht; M.B. Kuyper, general practitioner, Integraal Kankercentrum Oost; Nijmegen; G.M. Hesselmann, palliative care nurse specialist, University Medical Centre Utrecht

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Available in English and Dutch from the Association of Comprehensive Cancer Centres Web site.

Print copies: Available from the Association of Comprehensive Cancer Centres PO Box 19001, 3501 DA Utrecht, The Netherlands

AVAILABILITY OF COMPANION DOCUMENTS

A version of the guideline for Personal Digital Assistants (PDAs) is also available at the Association of Comprehensive Cancer Centres Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on May 8, 2008. The information was verified by the guideline developer on July 15, 2008.

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